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LAMBERTSON, DAVID A

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1636	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/815,300	Applicant(s) SYNOLD ET AL.	
	Examiner David A Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-67 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-67 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, 8, 9, 13-15, 21-23, 63 and 64, drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity through administration of an SXR antagonist, thereby altering/reducing drug catabolism, altering/reducing intestinal efflux, altering/reducing drug biliary excretion and/or altering/increasing oral absorption of a drug, classified in class 435, subclass 7.1.

II. Claims 1-5, 7, 8, 10-12, 14, 16, 21, 24, 63 and 65, drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity through administration of an SXR agonist, thereby altering/increasing drug catabolism, altering/increasing intestinal efflux, altering/increasing drug biliary excretion and/or altering/ reducing oral absorption of a drug, classified in class 435, subclass 7.1.

III. Claims 1-4, 17, 21 and 25 (with respect to a ribozyme for SXR mRNA), drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity by altering SXR mRNA levels, classified in class 435, subclass 6.

IV. Claims 1-4, 18, 21 and 26 (with respect to antisense for SXR mRNA), drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity by altering SXR protein levels, classified in class 435, subclass 7.95.

V. Claims 1-4, 19, 21, 25 (with respect to a ribozyme for an mRNA for a co-activator of SXR) and 26 (with respect to antisense for an mRNA for a co-activator of SXR), drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity by altering SXR recruitment of a co-activator, classified in class 435, subclass 7.93.

VI. Claims 1-4, 20, 21, 25 (with respect to a ribozyme for an mRNA for a co-repressor of SXR) and 26 (with respect to antisense for an mRNA for a co-repressor of SXR), drawn to a method for modifying drug pharmacokinetics and/or multiple drug resistance by altering SXR activity by altering displacement of a co-repressor from SXR, classified in class 435, subclass 7.93.

VII. Claims 27-33, 34 and 35, drawn to a method for identifying drugs with improved pharmacokinetic properties by screening the ability to modulate SXR by monitoring the expression of an endogenous SXR regulated gene (MDR1, CYP2C8 and CYP3A4), classified in class 435, subclass 7.3.

VIII. Claims 27-33 and 36, drawn to a method for identifying drugs with improved pharmacokinetic properties by screening the ability to modulate SXR by monitoring the expression of a synthetic reporter gene, classified in class 435, subclass 7.95.

IX. Claims 27-33 and 37, drawn to a method for identifying drugs with improved pharmacokinetic properties by screening the ability to modulate

SXR by monitoring the expression of a chimeric gene, classified in class 435, subclass 7.3.

X. Claims 27-33, 38 and 39, drawn to a method for identifying drugs *in vitro* with improved pharmacokinetic properties by screening the ability to modulate SXR by monitoring co-activator recruitment, classified in class 435, subclass 7.93.

XI. Claims 27-33, 38 and 40, drawn to a method for identifying drugs *in vitro* with improved pharmacokinetic properties by screening the ability to modulate SXR by monitoring co-repressor displacement, classified in class 435, subclass 7.93.

XII. Claims 27-33, 38 and 41-43, drawn to a method for identifying drugs *in vitro* with improved pharmacokinetic properties by screening the ability to modulate SXR by monitoring the binding of SXR and/or SXR/RXR to their regulatory sequences, classified in class 435, subclass 6.

XIII. Claims 44, 51-54, 56, 59 and 62, drawn to a method of identifying drugs that do not modulate SXR activity while co-administering an agent that acts as an antagonist for SXR, classified in class 435, subclass 7.1.

XIV. Claims 44, 51-54, 57, 60 and 62, drawn to a method of identifying drugs that do not modulate SXR activity while co-administering an agent that acts as an agonist for SXR, classified in class 435, subclass 7.1.

XV. Claims 44, 51-54, 61 and 62, drawn to a method of identifying drugs that do not modulate SXR activity while co-administering an agent that does not activate SXR, classified in class 435, subclass 7.95.

XVI. Claims 45, 66 and 67, drawn to a drug with improved pharmacokinetic properties and which modulate the activity of SXR, classified in class 514, subclass 1.

XVII. Claim 45, drawn to a drug that does not modulate SXR activity, classified in class 514, subclass 1.

XVIII. Claims 46-48, drawn to a method of screening patients for responsiveness to a pharmacological agent by monitoring the expression of an endogenous SXR regulated gene (CYP3A4 and CYP2C8), classified in class 424, subclass 9.1.

XIX. Claims 46 and 49, drawn to a method of screening patients for responsiveness to a pharmacological agent by monitoring therapeutic effects, classified in class 424, subclass 9.1.

XX. Claims 46 and 50, drawn to a method of screening patients for responsiveness to a pharmacological agent by monitoring toxic effects, classified in class 424, subclass 9.2.

XXI. Claim 55, drawn to a method of chemotherapy by co-administering a drug that modulates SXR activity or expression, classified in class 424, subclass 9.2.

XXII. Claim 58, drawn to a method for increasing the effectiveness of a drug by co-administering an agent that modulates SXR activity and/or expression, classified in class 435, subclass 7.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions Group I and Group II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and modes of operation and are not disclosed as capable of use together. The method of Group I is directed to modifying drug pharmacokinetics or multiple drug resistance by altering the activity of SXR by reducing its effects (e.g., by using an antagonist). This method requires different steps directed towards a different outcome from Group II, which is directed to the opposite function, a method of modifying drug pharmacokinetics or multiple drug resistance by altering the activity of SXR by increasing its effects (e.g., by using an agonist). Because these methods use different steps and are directed towards different outcomes, the methods represent patentably distinct inventions.

Inventions Groups I and II are unrelated to Groups III-VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and are not disclosed as capable of use together. The methods of Groups I and II are directed to methods of modifying drug pharmacokinetics or multiple drug resistance by altering the activity of SXR by increasing or decreasing its effects using either an antagonist or an agonist, respectively. These methods require different method steps or modes of operation with respect to Groups III-VI, which alter the activity of SXR by altering mRNA levels (III), altering protein levels (IV), altering SXR/co-activator association (V) or altering SXR/co-repressor association (VI) as opposed to

using an agonist or antagonist. Because these methods are performed using different modes of operation, the methods are patentably distinct.

Inventions Groups III-VI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and are not disclosed as capable of use together. Groups III-VI claim methods of modifying the pharmacokinetics of a drug or multiple drug resistance by altering the activity of SXR by altering mRNA levels (III), altering protein levels (IV), altering SXR/co-activator association (V) or altering SXR/co-repressor association (VI). Because these methods are performed using different modes of operation, the methods are patentably distinct.

Inventions Groups I-VI and Groups VII-XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects are not disclosed as capable of use together. The methods of Groups I-VI are directed to methods of modifying drug pharmacokinetics or multiple drug resistance which is a different outcome than the methods of Groups VII-XII, which are directed to the identification of a drug with increased pharmacokinetics in terms of its ability to modulate SXR activity (which would generate a new drug, rather than modifying an already known drug). Because the methods are directed to different outcomes, the methods have different effects and are therefore patentably distinct.

Inventions Groups VII-XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and are not disclosed as capable of use together. The methods of Groups VII-XII require different methods steps concerning the manner in which the drug, in terms of an ability to modulate SXR activity, is identified. These steps include monitoring the expression of an endogenous SXR regulated gene (VII), the expression of a synthetic reporter gene (VIII), the expression of a chimeric gene (IX), the recruitment of a co-activator (X), the displacement of a co-repressor (XI) and the binding of SXR DNA response elements (XII). Because each of these methods requires these different method steps, the methods have different modes of operation and are therefore patentably distinct.

Inventions Groups I-XII and Groups XIII-XV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as capable of being used together. The functions of Groups I-VI is to modify the pharmacokinetics of a drug or the multiple resistance to a drug and the functions of Groups VII-XII is to identify a drug with improved pharmacokinetics in terms of its ability to modulate SXR activity. The methods of Groups XIII-XV are directed to the identification of drugs that do not modulate SXR activity, which is a

different outcome from the outcomes of Groups I-VI and VII-XII. Because the methods are directed towards different outcomes, these methods are patentably distinct.

Inventions Groups XIII-XV are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and are not disclosed as capable of being used together. The methods of Groups XIII-XV require different method steps such as the use of an antagonist to reduce the expression/activity of SXR (XIII), the use of an agonist to increase the expression/activity of SXR (XIV) and the use of an agent that does not affect SXR activity (XV). Because these Groups comprise different method steps, they have different modes of operation and are therefore patentably distinct.

Inventions Groups VII-XII and XVI are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the drug can be identified by any of the patentably distinct methods from Groups VII-XII.

Inventions Groups I-VI, XIII-XV and XVII-XXII are unrelated to Group XVI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as being capable of use together. Specifically,

none of the methods of Groups I-VI, XIII-XV and XVII-XXII are directed to the identification of a drug having improved pharmacokinetics and an ability to modulate SXR activity. Therefore, the inventions as claimed are patentably distinct.

Inventions Groups XIII-XV and XVII are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the drug can be identified by any of the patentably distinct methods of Groups XIII-XV.

Inventions Groups I-XII, XVI and XVIII-XXII are unrelated to Group XVII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as capable of being used together. Specifically, none of the methods of Groups I-XII, XVI and XVIII-XXII are directed to the identification of a drug that does not modulate SXR activity. Therefore, the inventions as claimed are patentably distinct.

Inventions I-XV and XVIII-XX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as capable of being used together. The methods of Groups XVIII-XX are directed towards screening patients for the effectiveness of a drug, whereas the methods

of Groups I-XV are directed to methods to modify the activity of a drug or multiple drug resistance (I-VI), the identification of drugs that affect SXR activity (VII-XII) or the identification of drugs that do not affect SXR activity (XIII-XV). Each of these methods is directed to a different outcome, therefore each method has a different effect and is patentably distinct.

Inventions Groups XVIII-XX are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operations and are not disclosed as capable of being used together. The methods require different method steps including monitoring the expression of an endogenous SXR regulated gene (XVIII), monitoring the therapeutic effect of a drug (XIX) and monitoring the toxic effect of a drug (XX). Because these Groups required different method steps they involve different modes of operation and are therefore patentably distinct.

Inventions Groups I-XV and XVII-XX are unrelated to Groups XXI and XXII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as capable of being used together. The methods of Groups XXI and XXII are directed towards a method of chemotherapy by co-administering a drug that modulates SXR activity and a method for increasing the effectiveness of a drug by co-administering a drug that modulates SXR activity,

respectively. These methods are directed to different outcomes than the methods of Groups I-VI (modifying pharmacokinetics of a drug), Groups VII-XII (identifying a drug that modulates SXR activity), Groups XIII-XV (identifying a drug that does not modify SXR activity) and Groups XVIII-XX (screening patients for responsiveness to a drug). Because these methods are directed to different outcomes, they have different effects and are therefore patentably distinct.

Inventions Group XXI and Group XXII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and are not disclosed as capable of being used together. The method of Groups XXI is directed towards a method of chemotherapy by co-administering a drug that modulates SXR activity and the method of Group XXII is directed to a method for increasing the effectiveness of a drug by co-administering a drug that modulates SXR activity. These two methods are directed to different outcomes, therefore they have different functions and are patentably distinct.

Claims 1-5, 8, 11, 14, 21 and 63 link(s) inventions Groups I and II. Claims 1-4 and 21 link(s) inventions Groups III-VI. Claims 27-33 link(s) inventions Groups VII-IX. Claims 27-33 and 38 link(s) inventions Groups X-XII. Claims 44, 51-54 and 62 link(s) inventions Groups XIII-XV. Claim 46 link(s) inventions Groups XVIII-XX. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s) for each group. Upon the allowance of the linking claim(s), the

restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Concerning claims 44 and 46, they are claimed in a Markush type format; however the members of the group do not possess unity of invention and instead are patentably distinct inventions recited in the alternative. The members of the group are different and patentably distinct from each other because each member is a different condition or process that is to be measured in an attempt to discern alterations in metabolism, therefore there is no functional relationship between the members of the group (See MPEP 803.02). Upon election of any Group that contains any of the aforementioned claims, Applicant is required to elect one of the members of the group set forth in the claim. For clarity purposes, the Office considers the following alternatives for Claim 44: (i) expression levels of CYP2C8/CYP3A4/MDR1, (ii) expression levels of a synthetic reporter, (iii) expression levels of a chimeric gene, (iv) co-activator recruitment, (v) co-repressor displacement, (vi) binding to SXR responsive elements.

This is not an election of species. For clarity purposes, the Office considers the following alternatives for Claim 46: (i) SXR mRNA levels, (ii) SXR protein levels, (iii) SXR co-activator levels, (iv) SXR/co-activator interactions, (v) SXR co-repressor levels, (vi) SXR/co-repressor interactions, (vii) SXR polymorphisms and mutations, (viii) expression of an endogenous SXR regulated gene and (ix) levels of an endogenous SXR ligand. This is not an election of species.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, as it particularly pertains to Groups that have the same class/subclass, the non-patent literature searches for each of the groups listed above would not be co-extensive in scope with respect to one and other, therefore a simultaneous search of all of the groups would be burdensome.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
December 16, 2002

PATENT EXAMINER